



Perelman

School of Medicine

UNIVERSITY of PENNSYLVANIA

October 24, 2013

Dear Committee Members,

We are delighted to submit this letter in strong support of Dr. Christopher Bonafide's application for a Mentored Patient-Oriented Research Career Development Award (K23) and confirm our commitment to serve as his primary mentor (Keren) and co-mentors (Nadkarni and Holmes). *We have been Dr. Bonafide's primary mentors since 2008.* The purpose of this letter is to outline the plan for this outstanding candidate's training and research career development.

Introduction

Our broad objective is to facilitate Dr. Bonafide's transition from a trainee to an independent research scientist, capable of successfully competing for R-series funding from the NIH. Dr. Bonafide's overall career goal is to emerge as an independent patient-oriented research scientist with expertise in (a) evaluating interventions to prevent in-hospital cardiac arrest, respiratory arrest, and other adverse events in hospitalized patients, (b) optimizing these interventions, and (c) translating interventions proven to be effective into clinical practice. His success in meeting these goals depends heavily on the opportunity to focus his efforts on research training and career development afforded by this K23.

Dr. Bonafide has already demonstrated tremendous potential to succeed in patient-oriented research. His research focus has been in the domain of rapid response systems, which combine tools to identify patient deterioration on inpatient wards with teams capable of quickly rescuing patients with signs of impending cardiac or respiratory arrest. In this K23 application, he has proposed a project focused on physiologic monitoring technology. This is a natural extension of his previous work, demonstrating his continued intense interest in discovering the weaknesses and adverse impacts of the early warning systems we use to identify patients with impending cardiac or respiratory arrest. Using video and rigorous direct observational methods, he will be the first investigator to evaluate alarm fatigue and errors resulting from monitor interruptions among ill children with existing and projected heart and lung failure. While he will focus on this high-risk population of children, his findings will be novel and important with widespread significance. In short, Dr. Bonafide is an ideal candidate for this award and is embarking on an innovative, important research pathway with a high level of institutional support. However, he is not yet at a point where he can compete successfully for independent funding, and he would greatly benefit from the time and support to focus on the career development plan outlined below. With this K23 award combined with our sincere commitment to his career development, his likelihood of becoming an independent patient-oriented research scientist is outstanding.

Organization of Mentoring

We have proposed a co-mentoring organizational structure to optimize the chance of success for this candidate. Dr. Keren has been Dr. Bonafide's primary mentor for the last 5 years and will continue to serve in this capacity. Dr. Keren will meet with him weekly during the outset and then at least every 2 weeks during the award period to discuss progress on research activities and the training plan. Given Dr. Bonafide's unique and distinct research interests, for the past 5 years Dr. Keren has mentored and, during the award period, will continue to mentor Dr. Bonafide as part of a multidisciplinary team. The team also includes Dr. Vinay Nadkarni, an intensivist in the CHOP Pediatric Intensive Care Unit (PICU) and an internationally-recognized patient-oriented research scientist in pediatric critical care medicine, and Dr. John Holmes, a national figure in clinical informatics education and an accomplished information scientist with expertise in clinical decision support systems, human-computer interaction, and the application of mixed methods in healthcare. The candidate will meet at least monthly with Dr. Nadkarni to (a) discuss any challenges with implementing the research protocol, (b) ensure that his research is appropriately framed in the context of new developments in critical care

medicine research, and (c) discuss relevant connections to new R01 opportunities. He will meet with Dr. Holmes at least monthly to review progress in his training objective in clinical informatics. *In years 3-5 of this award, Drs. Keren, Nadkarni, and Holmes will devote additional time specifically to mentoring Dr. Bonafide as he focuses on developing and refining R01 proposals.*

Mentoring Experience

Dr. Keren has a strong track record mentoring fellows and junior faculty. As Director of the Academic General Pediatrics Fellowship from 2003-2010, he successfully recruited and mentored a total of 7 fellows. As co-Director of the NICHD T32-funded Pediatric Hospital Epidemiology and Outcomes Research Training (PHEOT) program since 2010, he has recruited three new cohorts of fellows (8 in total). Since his hire in 2001, he has been the primary mentor for 9 fellows, who have gone on to attain academic positions at major academic medical centers, medical director positions at pharmaceutical companies, or leadership roles in government (including Dr. Patrick Conway, Chief Medical Officer of Center for Medicare and Medicaid Services). He also mentors multiple junior faculty members (primary mentor for Drs. Pamela Weiss, Christopher Bonafide, and Lisa McLeod and secondary mentor for Dr. Evan Fieldston), whose NIH career development awards (K23, K99R00, or K08) were funded (Drs. Weiss and McLeod), favorably scored awaiting funding (Dr. Fieldston), or in preparation for resubmission (Dr. Bonafide). As a Senior Scholar at Penn's Center for Clinical Epidemiology and Biostatistics (CCEB), he has mentored a total of 10 students over the last 10 years and continues to take on one new fellow pursuing the MSCE degree each year. In 2013 he was awarded the CHOP Outstanding Faculty Mentor Award, a testament to his commitment to mentoring junior faculty.

Dr. Nadkarni has mentored more than 100 postdoctoral fellows and physician-scientists. His success as a mentor resulted in recognition with the CHOP Outstanding Faculty Mentor Award in 2011. He is a faculty mentor and collaborator on two institutional NIH T32 awards (EMERGE in Emergency Medicine and Resuscitation, PHEOT in Clinical Effectiveness and Patient Safety). As the critical care fellowship director for CHOP from 2001-2007, he recruited and mentored more than 35 clinical and research fellows, many of whom have become leaders in the field (e.g. Bradley Marino, MD, MPP, MSCE: K23 and R01 awardee, currently Director of the Heart Institute Research Core at the University of Cincinnati; Athena Zuppa, MD, MSCE: T32, K23, and R01 awardee, currently Associate Professor of Anesthesiology and Critical Care at Penn; Richard Levy, MD: T32, K08 awardee, currently Associate Professor of Anesthesiology, Pediatrics, and Integrative Systems Biology and Director of Cardiac Anesthesia at George Washington University; Marilyn Morris, MD, MPH: K08 awardee, currently Assistant Professor of Pediatrics at Columbia University). Dr. Nadkarni currently mentors 6 junior faculty including 2 career development awardees (Robert Sutton, MD, MSCE: K23; Alexis Topjian, MD, MSCE: K23), several AHRQ patient safety award scientists (Akira Nishisaki MD, MSCE, R18, R03; Dana Niles MS, R18), and 4 additional preparing career development award proposals (Aaron Donoghue, MD, MSCE, Scott Weiss, MD, Julie Fitzgerald, MD, PhD, and Christopher Bonafide, MD, MSCE), 4 fellows, and 2 full-time international fellows. In 2013, he was awarded the AAP Section on Critical Care Distinguished Career Award.

Dr. Holmes has extensive experience as a mentor and academic leader. He directs the doctoral training program in epidemiology at Penn, and teaches courses in epidemiology, study design, and database management in the Center for Clinical Epidemiology and Biostatistics. He was recently named Associate Director of the newly-created Institute for Biomedical Informatics at Penn, and will be responsible for developing two new Master's degrees and a certificate program in biomedical informatics. Dr. Holmes currently mentors two junior faculty members including one who is preparing a career development award proposal, three fellows, and two PhD students. He has previously mentored seven fellows, seven PhD students, and four undergraduates. Notably, three of Dr. Holmes's former trainees are involved in investigative work, including Giang Nguyen, MD, MPH, MSCE (Assistant Professor of Family Medicine and Community Health at Penn), George Makar, MD, MSCE (Assistant Professor of Medicine at Penn), Suvimol Niyomnaitham, MD, MSCE (now a PhD student in epidemiology at Queensland University), and Belinda Rivera Lebron, MD, MSCE (Assistant Professor of Medicine at the University of Pittsburgh). In addition, Dr. Holmes has also mentored a master's student in computer science, Adrian Benton. Under his mentorship, Mr. Benton as developed a very strong research program in natural language processing, as evidenced by three first-author publications in leading informatics journals. Finally, Dr. Holmes has served as the co-mentor for the candidate, Christopher Bonafide, MD, MSCE, since 2008.

Career Development Plan

We have proposed a career development plan specifically customized to Dr. Bonafide's long-term career goal to become an independent patient-oriented research scientist focused on evaluating and translating effective

interventions to prevent in-hospital cardiac arrest, respiratory arrest, and other adverse events in hospitalized patients. We will build upon the foundation of formal training in epidemiology and biostatistics that he received in the MSCE program and focus on key training objectives with direct ties to skills needed for the performance of his specific aims and future R01 applications. These include time-to-event analysis, trial design, and clinical informatics. He will continue his training in the responsible conduct of research offered by CHOP. He will participate and share his findings in research seminars held by the CHOP Center for Pediatric Clinical Effectiveness, the CHOP Center for Biomedical Informatics, the Penn Center for Clinical Epidemiology and Biostatistics, and the Penn Research in Embedded Computing and Integrated Systems (PRECISE) Center. His proposed research will make full use of the knowledge gained from these rigorous training objectives and serve as the foundation for future studies aimed at improving the signal-to-noise ratio of physiologic monitors.

Dissemination of Research Findings

Reviewers of his first submission considered Dr. Bonafide's publication record to be "early, but emerging." Since his first submission, Dr. Bonafide has greatly improved his publication record. In calendar year 2013 alone, Dr. Bonafide has had 8 peer-reviewed manuscripts published or accepted for publication (4 first author, 3 middle author, and 1 senior author) and was first author on the first chapter entirely devoted to rapid response systems for Rogers' Textbook of Pediatric Intensive Care. There will be a strong emphasis on publication throughout the entire period of this K23 award. We have formed the specific goal of at least 2 first-author and a total of 4 manuscripts published during each year of the award period, although we suspect that he will far exceed this goal. In addition, we have set the benchmark of attending and presenting research findings in at least two national meetings per year beginning in the second year of the award period, which may include the Society of Critical Care Medicine Annual Congress, the Pediatric Academic Societies Annual Meeting, and the Society of Hospital Medicine Annual Conference.

Research Support

The Children's Hospital of Philadelphia Department of Pediatrics has committed institutional developmental funds to Dr. Bonafide to support his salary, research assistant support, and project funds for initial investigations. Dr. Keren has dedicated additional project funds to support Dr. Bonafide's pilot work through the Pennsylvania Health Research Formula Fund Award. The projects in the K23 proposal are designed to be feasible using only the project funds provided by the Career Development Award. Future project support is available through the NIH, AHRQ, PCORI, foundation grants, endowed chair funds, and pilot grant funding at CHOP and Penn.

Other Responsibilities

With the support of the Department of Pediatrics at CHOP, Dr. Bonafide will devote 75% effort (9 person-months) to research and career development during the K23 period. His clinical and teaching responsibilities will be limited to no more than 25% of his time, implemented as approximately 9 weeks per year as attending physician for the general pediatric inpatient teaching service. He will continue providing lectures and facilitating simulation exercises for medical students and residents focused on the recognition and stabilization of deteriorating patients and the treatment of cardiac and respiratory arrest, as he has done since 2007. These experiences will foster the development of new research ideas and ensure that his research activities remain patient-oriented.

Summary

The proposed career development plan will provide Dr. Bonafide with the protected time to enable him to progress to an independent investigator discovering, optimizing, and translating effective tools to prevent in-hospital cardiac arrest, respiratory arrest, and other adverse events. We are fully committed to the success of Dr. Bonafide, and we are confident that he will develop into an outstanding patient-oriented research scientist.

Sincerely,



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